

**What is claimed is:**

1. A method for producing an antibody fragment, comprising the steps of:
  - 5 1) preparing an expression vector comprising a gene encoding a light chain of the antibody fragment fused with a first *E. coli* signal sequence and a gene encoding a heavy chain of the antibody fragment fused with a second *E. coli* signal sequence;
  - 2) transforming a microorganism with the expression vector;
  - 10 3) culturing the transformed microorganism in a medium; and
  - 4) collecting the antibody fragment secreted from the transformed microorganism into the medium.
2. The method of claim 1, wherein the antibody fragment is derived  
15 from a chimeric antibody, a humanized antibody or a human antibody.
3. The method of claim 1, wherein the antibody fragment is selected from the group consisting of Fab, Fab', F(ab')<sub>2</sub> and scFv.
- 20 4. The method of claim 1, wherein each of the first and the second *E. coli* signal sequences is selected from the group consisting of *E. coli* thermostable enterotoxin signal sequence, outer membrane protein A signal sequence,  $\beta$ -lactamase signal sequence, Gene III signal sequence, PelB signal sequence and a derivative thereof.
- 25 5. The method of claim 4, wherein each of the first and the second *E. coli* signal sequences is the *E. coli* thermostable enterotoxin signal sequence derivative having the nucleotide sequence of SEQ ID NO: 17 or the *E. coli* outer membrane protein A signal sequence having the nucleotide sequence of SEQ ID  
30 NO: 23.
6. The method of claim 5, wherein each of the genes encoding the light chain and the heavy chain is fused with the *E. coli* thermostable enterotoxin signal sequence derivative, and a single promoter regulates the expression of the  
35 genes encoding the light chain and the heavy chain.
7. The method of claim 5, wherein each of the genes encoding the light

chain and the heavy chain is fused with the *E. coli* outer membrane protein A signal sequence, and a single promoter regulates the expression of the genes encoding the light chain and the heavy chain.

5           8. The method of claim 5, wherein the gene encoding the light chain is fused with the *E. coli* thermostable enterotoxin signal sequence derivative, the gene encoding the heavy chain is fused with the *E. coli* outer membrane protein A signal sequence, and a single promoter regulates the expression of the genes encoding the light chain and the heavy chain.

10           9. The method of claim 5, wherein the gene encoding the light chain is fused with the *E. coli* outer membrane protein A signal sequence, the gene encoding the heavy chain is fused with the *E. coli* thermostable enterotoxin signal sequence derivative, and a single promoter regulates the expression of the  
15           genes encoding the light chain and the heavy chain.

          10. The method of claim 5, wherein each of the genes encoding the light chain and the heavy chain is fused with the *E. coli* outer membrane protein A signal sequence, and two promoters independently regulate the expression of the  
20           genes encoding the light chain and the heavy chain.

          11. The method of any one of claims 6 to 10, wherein the promoter is T7 promoter or Tac promoter.

25           12. The method of claim 1, wherein the antibody fragment is a fragment of anti-tumor necrosis factor-alpha.

          13. The method of claim 1, wherein the expression vector is selected from the group consisting of psDLHF\_B, psDLHF\_Bp, poDLHF, poDLHF\_B/S, pmsDLHF\_N/S and pmsDLHF\_S/K.  
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          14. The method of claim 1, wherein the microorganism is *E. coli*.

35           15. The method of claim 14, wherein the microorganism transformed with the expression vector is selected from the group consisting of *E. coli* BL21(DE3)/psDLHF\_B(HM10920) (KCCM-10509), *E. coli* BL21(DE3)/psDLHF\_BP(HM10921) (KCCM-10510), *E. coli*

BL21/poDLHF(HM10922) (KCCM-10511), BL21/poDLHF\_B/S(HM10923) (KCCM-10512), *E. coli* BL21/pmsDLHF\_N/S(HM10924) (KCCM-10513) and *E. coli* BL21/pmsDLHF\_S/K(HM10925) (KCCM-10516).

5           16. An expression vector comprising a gene encoding a light chain of an antibody fragment fused with a first *E. coli* signal sequence and a gene encoding a heavy chain of the antibody fragment fused with a second *E. coli* signal sequence, wherein the antibody fragment expressed from the expression vector is secreted into a culture medium.

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          17. The expression vector of claim 16, wherein the antibody fragment is derived from a chimeric antibody, a humanized antibody or a human antibody.

          18. The expression vector of claim 16, wherein the antibody fragment is  
15       selected from the group consisting of Fab, Fab', F(ab')<sub>2</sub> and scFv.

          19. The expression vector of claim 16, wherein each of the first and the second *E. coli* signal sequences is selected from the group consisting of *E. coli* thermostable enterotoxin signal sequence, outer membrane protein A signal  
20       sequence,  $\beta$ -lactamase signal sequence, Gene III signal sequence, PelB signal sequence and a derivative thereof.

          20. The expression vector of claim 19, wherein each of the first and the second *E. coli* signal sequences is the *E. coli* thermostable enterotoxin signal  
25       sequence derivative having the nucleotide sequence of SEQ ID NO: 17 or the *E. coli* outer membrane protein A signal sequence having the nucleotide sequence of SEQ ID NO: 23.

          21. The expression vector of claim 20, wherein each of the genes  
30       encoding the light chain and the heavy chain is fused with the *E. coli* thermostable enterotoxin signal sequence derivative, and a single promoter regulates the expression of the genes encoding the light chain and the heavy chain.

35           22. The expression vector of claim 21, wherein the antibody fragment is a fragment of anti-tumor necrosis factor- $\alpha$ .

23. The expression vector of claim 22, wherein the single promoter is T7 promoter.

24. The expression vector of claim 23, which is psDLHF\_B or  
5 psDLHF\_Bp.

25. The expression vector of claim 20, wherein each of the genes encoding the light chain and the heavy chain is fused with the *E. coli* outer membrane protein A signal sequence, and a single promoter regulates the  
10 expression of the genes encoding the light chain and the heavy chain.

26. The expression vector of claim 25, wherein the antibody fragment is a fragment of anti-tumor necrosis factor-alpha.

15 27. The expression vector of claim 26, wherein the single promoter is Tac promoter.

28. The expression vector of claim 27, which is poDLHF.

20 29. The expression vector of claim 20, wherein each of the genes encoding the light chain and the heavy chain is fused with the *E. coli* outer membrane protein A signal sequence, and two promoters independently regulate the expression of the genes encoding the light chain and the heavy chain.

25 30. The expression vector of claim 29, wherein the antibody fragment is a fragment of anti-tumor necrosis factor-alpha.

31. The expression vector of claim 30, wherein the promoter is Tac promoter.

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32. The expression vector of claim 31, which is poDLHF\_B/S.

33. The expression vector of claim 20, wherein the gene encoding the light chain is fused with the *E. coli* thermostable enterotoxin signal sequence derivative, the gene encoding the heavy chain is fused with the *E. coli* outer  
35 membrane protein A signal sequence, and a single promoter regulates the expression of the genes encoding the light chain and the heavy chain.

34. The expression vector of claim 33, wherein the antibody fragment is a fragment of anti-tumor necrosis factor-alpha.

5 35. The expression vector of claim 34, wherein the single promoter is Tac promoter.

36. The expression vector of claim 35, which is pmsDLHF\_N/S.

10 37. The expression vector of claim 20, wherein the gene encoding the light chain is fused with the *E. coli* outer membrane protein A signal sequence, the gene encoding the heavy chain is fused with the *E. coli* thermostable enterotoxin signal sequence derivative, and a single promoter regulates the expression of the genes encoding the light chain and the heavy chain.

15 38. The expression vector of claim 37, wherein the antibody fragment is a fragment of anti-tumor necrosis factor-alpha.

20 39. The expression vector of claim 38, wherein the single promoter is Tac promoter.

40. The expression vector of claim 39, which is pmsDLHF\_S/K.

25 41. A microorganism transformed with the expression vector of claim 16.

42. The microorganism of claim 41, which is *E. coli*.

30 43. The microorganism of claim 42, which is selected from the group consisting of *E. coli* BL21(DE3)/psDLHF\_B(HM10920) (KCCM-10509), *E. coli* BL21(DE3)/psDLHF\_BP(HM10921) (KCCM-10510), *E. coli* BL21/poDLHF(HM10922) (KCCM-10511), *E. coli* BL21/poDLHF\_B/S(HM10923) (KCCM-10512), *E. coli* BL21/pmsDLHF\_N/S(HM10924) (KCCM-10513) and *E. coli* BL21/pmsDLHF\_S/K(HM10925) (KCCM-10516).

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